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Magnesium and Memory: Unraveling the Physiological Tapestry of Alzheimer's Disease

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Alzheimer disease is the leading cause of Dementia throughout the world. There are multiple researches are undergoing globally to understand the etiology of this disabling disease. Magnesium is another suspicious factor that might produce this disease.

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Objectives: The study was aimed to evaluate possible association between serum magnesium and Alzheimer disease.
Methodology: This case control study was conducted in the emergency Department in collaboration of Medical OPD of Liquate University Hospital Hyderabad from January 2023 to December 2023. 300 participants were divided into control, 200 participants and 100 in the test group. Serum Magnesium was evaluated into both control and test group. Graph Pad Prism 9 was used to detect P value. Significance of variable was considered below 0.05.
Results: Those who were suffering from Alzheimer disease shows more Hypomagnesaemia (p-value= 0.001) than normal patients. The low serum Magnesium level was found 3.1 times greater (Odds ratio= 5.5, likelihood ratio= 1.9) in Alzheimer patients
Conclusion: there is a specific association between Hypomagnesaemia and Alzheimer disease.

Keywords: Alzheimer disease; serum magnesium; dementia.

1. INTRODUCTION

Alzheimer disease (AD) is a neurological disorder in which there is impairment in cognition and language comprehension [1]. Worldwide prevalence of Alzheimer diseases is nearly about 24 million and the risk of incidence get double after 65 years of age [2]. It is an estimate that 50 million peoples are suffering from this disease globally and it will rise to 150 million by the year 2050 [3]. Globally a huge amount is spent on the treatment of dementia.in 2015 55 million dollars and in 2030 2 trillion dollars will be be the cost of treatment [4].

Alzheimer is a defect in the cognition of brain caused by the patchy deposition of amyloid proteins in the neurons of hippocampus and cerebellar cortex which obstructs neuronal communication leading to neuronal death [5]. The most common symptoms of Alzheimer's disease is impairment of short term memory and later on problem solving capacity, language integration behavior change occur [2].

It is found that a specific protein as p-STAT3-Tyr705 and were found increased in the signaling pathway called JAK2/STAT [6]. Once the brain parenchyma is damaged, the glial cells receive signals of the damage, which triggers the tau protein, causing it to undergo hyper phosphorylation and oligomerization inside the axon. Additional axon damage results from this alteration in the tau protein's typical shape, leading to cognitive impairment [7].

Magnesium is a crucial part of cells glucose transport system which maintains cell integrity [8]. The transport system across the cell membrane is dependent upon ATPASE enzyme system which need magnesium ion for its proper functioning [9]. The concentration level of magnesium in CSF is much greater than concentration level in plasma [10]. Multiple researches proves that hypomagnesaemia causes neuronal damage which leads to cognitive dysfunction [11]. Magnesium plays an important role in integrity of cardiovascular system while alzihmer is basically caused by the disintegration of vascular system of neurons [12]. The required amount of Magnesium in blood maintains structural and physiological integrity of synapse by which it enhance and improves the ability of hippocampus to restore memory [13].

The normal range of magnesium in a healthy adult is between 0.70 mM to 1.05 mM. The synapses in hippocampus are quite sensitive to the fluctuations in magnesium concentration. Therefor an increase in half of magnesium concentration wills double the density of synapse [14]. Hypomagnesaemia is a potential risk factor for dementia, hypertension, cerebrovascular accidents, and thrombotic plaques [15].

After extensive clinical experimentation on rodents it has been discovered that those pharmaceutical drugs which increase the concentration of magnesium in brain like (MgT), helps in regaining the ability to retain memory by increasing NMDR receptor signaling pathway and preventing degradation of synapses [16].

The data which is gathered after performing several autopsies of alzihmer patients brain indicates a lower gradient of magnesium as compared to a healthy individual [17]. NMDA receptors in brain are responsible for maintain synaptic transmission plasticity and neuronal modulation. While the excessive stimulation of these receptors causes excitotoxicity which leads to cell death. Magnesium prevents the over excitably of these receptor therefore

hypomagnesaemia leads to increase incidence of alzihmer [18].

The ultimate objective of the current investigation was to explore into any potential connections between Alzheimer's disease and hypomagnesemia, with the emphasis on Hyderabad, Sindh's population.

2. METHODOLOGY

The current study was a case control study which was undergone in the Department of emergency medicine of Liquate university hospital Hyderabad from January 2023 to December 2023 after approval from Ethical Review Committee of department of Physiology and MLT of Sindh university Jamshoro Sindh Pakistan with MR . no 127 and permission of the study was also taken from the in charge of Department Of Emergency Medicine Of Liquate University Hospital, Hyderabad, Sindh, Pakistan . The study comprised of 300 patients who came into the department. The participants were divided into two groups, a control group of 200 participants who were not suffering from dementia and 100 participants in the study group suffering from dementia. The age group of patients was 60 and above 6o years. All those patients who were taking laxative, diuretics, alcohol and any other disease which can affect serum magnesium level were excluded.

Before the conduction of study participants were clearly explained about the purpose of study. A written consent was taken from all the participants. Three milliliter of blood was drawn from a visible vein using the aseptic technique, and the blood was then transfused into a test tube that had a red rubber top. It was forwarded to the research lab right away. The serum magnesium level was estimated using a Roche C311 auto analyzer.

Rosanoff A, West C et al. study establishes reference points for hypo- and hypermagnesemia as well as standard values for normal serum magnesium levels. The serum magnesium level is 0.73-1.06mmoL/1.8-2.6mg/dL in male and 0.77-1.03 mmoL/1.9-1.03mg/dl. Serum level below 2.07 mg/dL was taken as hypo magnesia and more than 2.5mg/dL was taken as hyper magnesia.

The Alzheimer disease was diagnosed by the criteria laid down by the National Institute on Aging-Alzheimer's Association (NIA-AA) which included neuroimaging, Biomarker of cerebrospinal fluid and assessment of cognition.

Statistical analysis was conducted through Graph Pad Prism 9.the significance between variable was evaluated by P value less than 0.05. Descriptive statistics and Chi-square tests were applied to evaluate the Data.

3. RESULTS

Table 1. Frequency of age of participants

Gender	Total number	Average
Male	230	77%
Female	70	23%
Total	300	100%

Table 1 describes Age frequency of participants. According to table there were a total of 300 individuals, 77% are male, 23% are female, and the total percentage adds up to 100%.

Table 2 describes the Mean age was 72±6.55, Median 72, 75 Percentile was 76, CI was 71.5-73.01, Minimum age was 60 years and Maximum was 87 years.

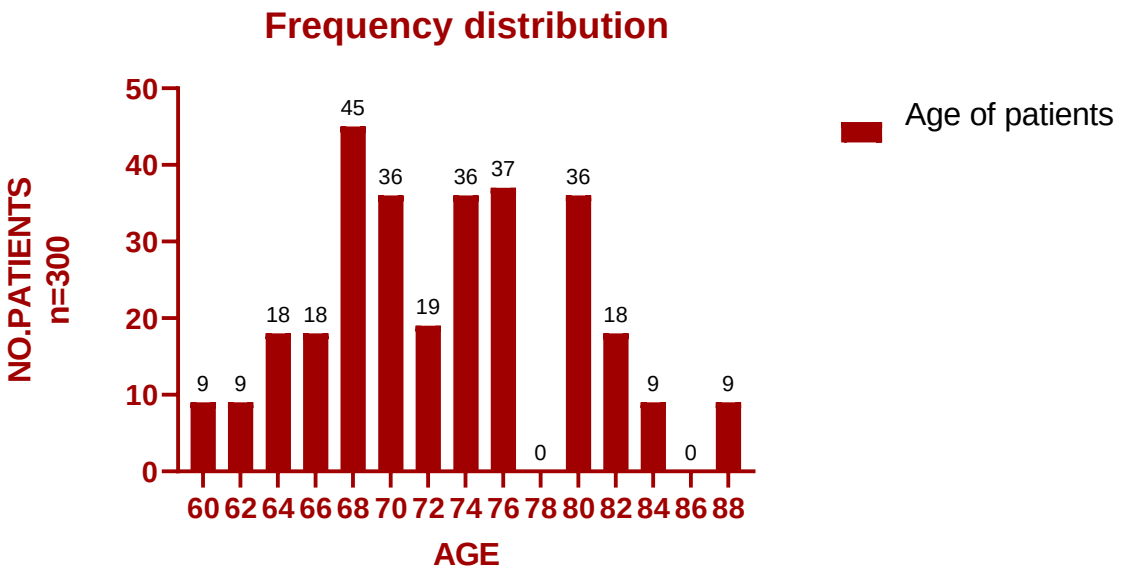
Table.3 and Graph. 2; delineates a noteworthy distinction between levels of serum magnesium among normal individuals (n=200) and those diagnosed with Alzheimer's disease (N=100), showing that hypomagnesaemia is more prevalent in alzehmeirs patients, that also statistically supported by (odds ratio =5.5) showing that low serum magnesium levels is 5.5 times more prevalent in alzehmeirs patient in comparison to normal individual.

Table 2. Descriptive statistics of age of participants

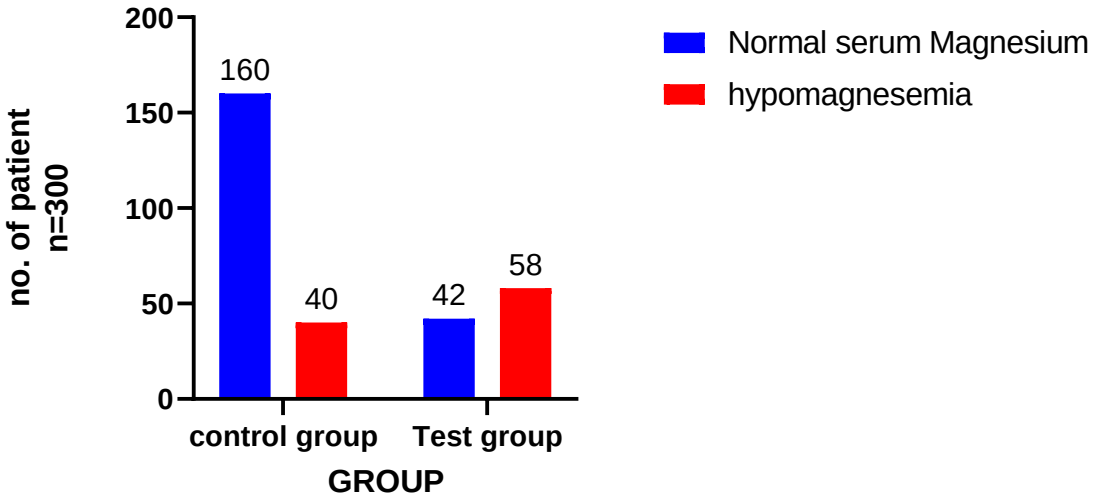
Number of patients	Mean	Median	75 Percentile	CI	Minimum	Maximum
300	72.26±6.55 years	72y	76	71.5-73.01	60 y	87y

Table 3. Serum magnesium level in normal versus alzheimer patients

Type of Patients	Normal Serum Magnesium	Hypomagnesaemia	Total	P value	R/R	Odd/R	likehoodRatio	Sensit/Speciv
Normal	160	40	200	0.001	1.90	5.52	1.94	0.79/0.59
n=200	53.33%	13.33%	66.66%					
Alzheimer Disease	42	58	100					
N=100	14%	19,33%	33.33%					
Total	202	98	300					
N=300	67.33%	32.66%	100%					



Graph 1. Describes the descriptive statistics of age



Graph 2. Distinction between levels of serum magnesium among normal individuals

4. DISCUSSION

Several studies throughout the world have investigated the relationship between serum magnesium level and the etiology of Alzheimer diseases. A consensus seems to be emerging globally regarding a potential impact of low serum Magnesium level on the cognition ability.

The current study concluded that low serum Magnesium level was observed in Alzheimer disease,19% participants showed relevance between low serum magnesium and Alzheimer disease. The *P* value was 0.001 showing significance between the two variables. Serum magnesium prevent the over excitation of NMDA receptors. The deficiency of magnesium initiate a cascade of inflammation in the neurons due to release of inflammatory mediators e.g. interleukin 4 and tumor necrosis factor leading to neurodegeneration. Amyloid β-protein is the basic cause of Alzheimer disease, the excess of which is inhibited by serum magnesium [19].

This relation of hypomagnesaemia in causing cognitive impairment in Alzehmeirs patient is also supported by study results conducted by Lei Dy etal with P value of 0.001 [20]. Further more Maier JAM also showed that correcting the magnesium levels in Alzehmeirs patients will prevent cognitive impairment in Alzehmeirs patients [21]. In a recent study conducted by Kateba Al etal in2020 stated that low serum Magnesium level by inhibiting GSK-3β I protect the synaptic function and plasticity. Showing that low serum level of Magnesium leads to Neurodegeration and synaptic disintegration. In another study conducted by Jasper et al in 2021 concluded that magnesium deficiency leads to neuronal damage and genesis of Alzheimer disease [22].

There are other factors besides altered levels of magnesium that plays pivotal role in developing congnitive impairment that include family history supported by study results of Gao etal that patients with family history of dementia are more likely to have congintive impairment than patient with normal family history (p=0.0009) [23].

The study raises the need for further evaluation of a possible link between serum Magnesium and Alzheimer disease

5. CONCLUSION

The study concludes that there is a strong relationship between low serum Magnesium and Alzheimer diseases showing that low serum magnesium level is more prevalent in alzehmeirs patient (19.33%) in compare to normal individual (13.33%), further supported statistically by odd ratio =5.5 , i.e. alzehmeirs patient are 5.5 time more likely to have low serum magnesium level than normal individual.

ETHICAL CONSIDERATION

The current study was conducted according to Helsinki accord.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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